



Pathogenesis, evaluation, and management of osteolysis after total shoulder arthroplasty

Kyle N. Kunze^{1,2}, Laura M. Krivicich³, Christopher Brusalis^{1,2}, Samuel A. Taylor^{1,2}, Lawrence V. Gulotta^{1,2}, Joshua S. Dines^{1,2}, Michael C. Fu^{1,2}

¹Department of Orthopedic Surgery, Hospital for Special Surgery, New York, NY, USA

²Sports Medicine Institute, Division of Shoulder and Elbow, Hospital for Special Surgery, New York, NY, USA

³University of Illinois College of Medicine, Chicago, IL, USA

Radiographic osteolysis after total shoulder arthroplasty (TSA) remains a challenging clinical entity, as it may not initially manifest clinically apparent symptoms but can lead to clinically important complications, such as aseptic loosening. A thorough consideration of medical history and physical examination is essential to rule out other causes of symptomatic TSA—namely, periprosthetic joint infection—as symptoms often progress to vague pain or discomfort due to subtle component loosening. Once confirmed, nonoperative treatment of osteolysis should first be pursued given the potential to avoid surgery-associated risks. If needed, the current surgical options include glenoid polyethylene revision and conversion to reverse shoulder arthroplasty. The current article provides a comprehensive review of the evaluation and management of osteolysis after TSA through an evidence-based discussion of current concepts.

Keywords: Total shoulder arthroplasty; Osteolysis; Complications; Aseptic; Loosening; Shoulder

INTRODUCTION

The annual incidence of primary anatomical and reverse shoulder arthroplasty (RSA) procedures performed in the United States has increased by 103.7% between 2011 to 2017, with the incidence of RSA increasing 191.3% over the same time period [1]. Though reproducible and efficacious procedures for glenohumeral osteoarthritis, rotator cuff arthropathy, and proximal humerus fractures, studies examining the outcomes of both anatomical total shoulder arthroplasty (TSA) and RSA at long-term follow-up report average revision rates of approximately 8%–10%

[2–4]. Radiographic osteolysis and glenoid loosening are the most common complications after TSA, accounting for 80% of TSA complications and 7% of revision operations, respectively, while humeral loosening accounts for a much smaller 7% of long-term TSA complications [5]. Therefore, a comprehensive understanding of the mechanisms leading to osteolysis and careful evaluation of patients presenting with osteolysis after TSA is critical.

Gradual osteolysis around the glenoid or humeral components and loosening of either the glenoid or humeral components can result in instability and loss of function [6]. Furthermore, osteol-

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Correspondence to: Kyle N. Kunze

Department of Orthopedic Surgery, Hospital for Special Surgery, 535 E. 70th St, New York, NY 10021, USA

Tel: +1-609-214-9245, E-mail: KunzeK@hss.edu, ORCID: <https://orcid.org/0000-0002-0363-3482>

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ysis with or without component loosening may be a primary cause of pain, necessitating revision [7]. Therefore, osteolysis around the glenoid or humeral components is not a clinically insignificant entity, as it may lead to additional morbidity and health resource utilization. Despite this knowledge, a comprehensive resource of management options and current concepts in addressing these adverse events is lacking. As such, it is imperative for the most recent literature pertaining to the evaluation and management of osteolysis after TSA to be synthesized and reviewed to better understand the available options for this challenging clinical scenario and optimize patient outcomes.

The purpose of the current article is to present a comprehensive review of the current concepts in the pathogenesis, evaluation, and management of osteolysis after anatomical TSA and RSA. In the first half of this article, the pathogenesis of osteolysis and the evolution in implant design intended to avoid osteolysis are presented. In the second half of this article, we discuss our approach to evaluating and managing osteolysis treatment through an evidence-based analysis of the literature.

This study did not require approval by the institutional review board at the Hospital for Special Surgery. And, consent was not required for any aspects of this study.

PATHOGENESIS OF OSTEOLYSIS

Implant Wear and Immune Response

Implant wear occurs primarily at the articular interface, generating debris that results in the destruction of surrounding tissue secondary to inflammation. The destruction is two-fold: damage to the articulating surface of the prosthesis can be detrimental to implant stability, and the debris generated by implant wear can drive inflammation [8]. Debris may originate from multiple implant compositions, including polyethylene, metal, and cement. Generated debris can then implant on the articular surface of a polyethylene prosthesis, further exacerbating implant wear by enhancing abrasion [9].

Phagocytosis of debris less than twelve 12 μ m micrometers in diameter by macrophages underlies the primary pathogenesis of periprosthetic osteolysis; however, the specific inflammatory response is dictated by the quantity and quality of the particulates regarding size, surface area, and composition. Further, the relative concentration of debris, rather than simply the number of particles, dictates the magnitude of the inflammatory response [10,11]. Macrophage stimulation after debris phagocytosis results in the release of tumor necrosis factor-alpha (TNF- α), interleukin (IL)-1 β , and IL-6. TNF- α and IL-6 are catabolic mediators in bone, and IL-1 β induces the differentiation of osteoclasts and the

production of matrix metalloproteinases that promote bone resorption [11,12]. Polyethylene debris is also associated with complement (CR3) activation, resulting in more macrophage recruitment [13].

Cement debris resulting in larger particulates not amenable to phagocytosis is associated with giant cell recruitment and toll-like receptor (TLR) stimulation, which, in turn, activates the inflammatory nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) cascade [14]. The receptor activator of nuclear factor-kappa-B (RANK) and its ligand (RANKL) bind on preosteoclasts, stimulating osteoclastogenesis via the NF- κ B transcription factor pathway and, in turn, causing bony resorption. As such, NF- κ B is the transcription factor most commonly implicated in osteolysis; it is activated by several mechanisms, including those mediated by TLRs, TNF- α , and IL-1 [15,16]. In summary, periprosthetic osteolysis, characterized by concomitant inflammation, fibrosis, and bony resorption, occurs as an aseptic chronic inflammatory response to intra- and periarticular debris.

Histology

Histologic findings of periprosthetic osteolysis include inflammatory cells (lymphocytes, histiocytes, plasma cells, giant cells, and macrophages), which may contain identifiable particulate debris; clefts containing strongly birefringent polyethylene debris; and scalloped edges where cement has been resorbed. Interestingly, Kepler et al. [9] reported no significant difference in the frequency of polyethylene debris between patients with and without osteolysis after anatomical TSA (62% vs. 67%), indicating that the presence of particles alone is not predictive of osteolysis [9]. In cases of osteolysis in the absence of debris on histologic analysis, the pathogenesis of bone loss is currently unknown.

Detritic synovitis is an inflammatory response to intraarticular debris, which causes more widespread osteolysis beyond the periprosthetic space, resulting in implant loosening or pathologic fracture [17]. Known to cause implant failure in hip, hand, and foot arthroplasty, detritic synovitis leading to osteolysis after anatomical TSA was first described in 2018 [17-19]. Guild et al. [20] described an inflammatory foreign body reaction to polyethylene implant wear resulting in osteolysis; histopathologic analysis found multinucleated giant cell and histiocyte infiltrates and polarizable debris resulting from the destruction of bone and joint tissue. Detritic synovitis and periprosthetic osteolysis share many histological characteristics; however, the scope of their consequences differs given the relative lack of geographic limitation seen in detritic synovitis.

MICROMOTION

High amplitude micromotion increases the abhorrent space between the prosthesis and bone, resulting in fibrous ingrowth [21]. Though the threshold at which micromotion may be of benefit is contested [21-23], the enlarged periprosthetic space seen with higher amplitude micromotion allows for a less coherent bone-implant interface where synovial fluid and wear particles may enter and stimulate inflammation, causing bony resorption, further weakening the bone stock via osteolysis and promoting further implant loosening [24].

Several biomechanical studies have investigated the implications of high amplitude micromotion on the glenoid component in both anatomical TSA and RSA, although *in vivo* analyses are scarce. Sabesan et al. [25] created a biomechanical model to study the influence of increasing glenohumeral implant mismatch on bone-implant interface micromotion. The authors reported that a radial mismatch of greater than 10 mm between glenohumeral components increased the micromotion of an all-polyethylene pegged glenoid component. Bonneville et al. [26] reported 20–130 μm of micromotion was found across three separate modern RSA glenoid baseplates, demonstrating that adequate stability was achieved by all models on finite element analysis. Lung et al. [27] found that decreased micromotion of the RSA glenoid baseplate was associated with longer central pegs and longer peripheral screws in general, but no absolute arrangement of screws appears to be superior in optimizing RSA baseplate fixation and decreasing micromotion [28,29]. Chou et al. [30] reported increased micromotion with the use of eccentric glenospheres in RSA when compared to the same-sized concentric design, although eccentric designs were still associated with micromotion amplitudes in the range in which bony ingrowth was possible. Together, these results suggest that, while osteolysis and aseptic glenoid loosening remain the most common reason for failure after anatomical TSA, primary micromotion of the glenoid component is a much less common cause of failure when modern RSA designs are implemented.

NOTCHING

Notching of the inferior border of the scapula was historically a considerable source of osteolysis in RSA, though the development of lateralized glenospheres and increased awareness of the importance of glenoid positioning has decreased the incidence of this phenomenon. Mechanical notching is described as repetitive contact between the humeral implant and scapula, leading to progressive abrasive wear [31]. This wear often leads to biological

notching, whereby debris is generated through active osteolysis that may further accelerate notching [32]. With continued notching and osteolysis, catastrophic failure of the glenoid component fixation can occur [33].

Implant Components and Design

Variations in component composition, component positioning, and stem length have been the mainstay approach to reducing implant wear and associated debris, inflammation, and osteolysis. Cemented all-polyethylene glenoid components are associated with 83% or greater survival rates at year 10 of follow-up; however, wear and revision rates vary between polyethylene models [34,35]. Cross-linked polyethylene has been associated with an 85% reduction in wear rates relative to traditional polyethylene components as well as lower revision rates at year 5 of follow-up [36,37]. Metal-backed glenoid components are associated with substantially lower survival rates at long-term follow-up than all-polyethylene glenoid components, with failure attributed to aseptic loosening in the all-polyethylene group and rotator cuff insufficiency and instability in the metal-backed group [38]. Hybrid glenoid implants, which feature porous metal central posts and no metal backing to the glenoid surface, have not been associated with significant differences in complication rates at year 3 of follow-up relative to all-polyethylene implants [39]. Friedman et al. [40] report that the hybrid glenoid component is superior to the all-polyethylene implants with regard to 3-year revision rates, though longer-term investigations on the longevity of these implants are still needed.

Research investigating the means to reduce osteolysis surrounding humeral implants has largely focused on stem length and implant composition. Bell et al. [41] demonstrated decreased rates of radiolucent lines and humeral osteolysis in stemless ceramic humeral components when compared to long-stem metal-head alternatives. Long-stem designs are associated with stress shielding of the proximal humeral metaphysis, resulting in increased bone resorption, while the opposite is true for stemless humeral component designs. Indeed, stemless designs have been demonstrated to better mimic intact bone [42,43]. Investigations of humeral implant composition have demonstrated a decreased wear rate associated with ceramic humeral heads when compared to metallic components [44].

CLINICAL EVALUATION

History and Physical Exam

Comprehensive postoperative follow-up and physical evaluation should be performed in the setting of new-onset pain following

TSA regardless of the time from the index procedure. The most sensitive indicator of osteolysis following TSA is new-onset or persistent pain [9]. However, postoperative pain is non-specific and should prompt a comprehensive evaluation of other etiologies. Other considerations that may induce pain after TSA include periprosthetic infection, periprosthetic fracture, stiffness, rotator cuff pathology, heterotopic ossification, bursitis, and malalignment. It should be determined whether the pain is associated with weakness or decreased motion, as this may leverage insight into additional shoulder stabilizer involvement and displacement of the glenoid or humeral components.

Importantly, the timing, quality, responsiveness, location, and duration of symptoms can provide more insight into the potential pathology. For example, pain secondary to glenoid or humeral osteolysis is generally experienced when sleeping or first initiating movement (start-up pain) of the shoulder and is diffuse in nature, whereas well-localized pain over the posterosuperior aspect of the shoulder may represent an acromial stress fracture. Pain in the proximal part of the upper extremity can indicate humeral component loosening. Patients should also be asked about wound issues and drainage after the index surgery, as this may elevate indolent infection as a cause of symptoms. Concern for possible osteolysis and aseptic loosening should be raised for patients who report years of symptom-free shoulder function postoperatively followed by new-onset pain or reduced function.

The physical exam should be performed systematically and include inspection, palpation, range of motion, strength, and provocative maneuvers where appropriate. Specifically, the surgical incision and skin around the shoulder should be assessed. The presence of effusion, erythema, or swelling may indicate chronic inflammation or infection. Diffuse tenderness to palpation around all areas of the shoulder in the absence of other findings may signify a chronic pain syndrome.

The extent of passive and active range of motion should be assessed, with particular attention directed towards instability, impingement, or pain along short arcs of motion. Patients with osteolysis that begin to experience early subsidence may experience loss of function. Atrophy or deformity in the setting of a primary anatomical TSA may suggest compromise of the rotator cuff. Finally, a thorough neurovascular exam should be assessed to rule out neurovascular compromise as the etiology of pain and dysfunction.

Though osteolysis is characteristically a chronic process associated with night or start-up pain, it is notable that early osteolysis may manifest non-characteristic symptoms. Therefore, in the setting of painful TSA, early osteolysis should still be considered with a thorough evaluation of routine radiographic imaging. In-

deed, early osteolysis that is rapidly progressive without identification and treatment can result in glenoid loosening, subsidence, and early failure.

In all scenarios where a patient presents with a painful TSA, standard laboratory testing including complete blood count, erythrocyte sedimentation rate, and C-reactive protein measurement should be obtained. If these raise suspicion for infection, such as if the synovial leukocyte count exceeds 2,000 and is composed of at least 70% polymorphonuclear leukocytes [45], an ultrasound-guided shoulder aspiration is warranted. However, in cases with a high index of suspicion for infection but negative laboratory and aspiration work-up, arthroscopic or open tissue biopsy is considered a gold standard diagnostic tool for infection. If periprosthetic joint infection has been ruled out, osteolysis and aseptic loosening then rise among the differential diagnoses as the culprit of shoulder pain [46].

Radiographic Evaluation

Postoperative radiographs are the first-line imaging modality to evaluate for osteolysis in the proximity of either the glenoid or humeral components. Standard views of the shoulder, including anteroposterior, Grashey, lateral, and axillary views, should be obtained. The examiner should evaluate radiographs for radiolucencies and stress shielding adjacent to the glenoid and humeral components. Comparison to prior radiographs should be made when available, particularly when monitoring the progression of previously diagnosed osteolysis. The examiner may observe implant loosening, malpositioning, or subsidence. Particular attention should be focused on the location of the humeral head, as proximal migration may indicate a supraspinatus tear, and anterior displacement may suggest a tear of the subscapularis.

In non-cemented humeral components, radiolucent lines often occur at the tip of the prosthesis, whereas radiolucencies commonly develop along the proximal and midbody aspects of the stem in cemented humeral components. In some smaller series with 10 years of follow-up, over 50% of patients developed radiolucencies, most often in association with glenoid wear and polyethylene debris [47]. However, the clinical significance of osteolysis remains unclear in certain populations, as asymptomatic patients with osteolysis do not always require a revision procedure [48].

It also appears that the choice of humeral fixation technique is not associated with osteolysis on radiographs. A recent randomized controlled trial with a mean 38-month follow-up period reported a 0.74% incidence of radiolucencies ≥ 2 mm in three or more zones, which did not significantly differ between cemented and non-cemented humeral component cohorts [49]. Scapular

notching may be a more obvious finding of progressive osteolysis. In a 10-year follow-up study of patients treated with a Grammont-style RSA, 73% of patients developed scapular notching on radiographs, with 12% having undergone revision surgery [50].

Unfortunately, radiolucent lines on plain radiographs do not always reliably diagnose loosening, particularly during long-term follow-up, as some series report the presence of radiolucent lines in up to 80% of radiographs at 10 years of follow-up [51]. Therefore, it may be more appropriate to evaluate radiolucent line progression over time, as opposed to making a definitive plan of care based on a single observation. Advanced imaging appears to be more sensitive than radiography at detecting radiolucency. Recent studies have demonstrated that the reliability of computed tomography (CT)-based assessments of radiolucencies is three times higher than that of radiographs, and up to 40% of radiolucent lines and 74% of osteolysis cases not observed on radiographs are detectable by CT [51,52].

In cases of osteolysis following RSA, notching of the polyethylene liner against the inferior border of the scapula should be assessed. This mechanical impingement can potentially lead to a high level of particulate debris, leading to osteolysis in both the glenoid and the humerus. In severe cases, significant osteolysis can occur at the inferior glenoid, directly affecting baseplate fixation. In the evaluation of osteolysis after RSA, component malposition should be recognized early and potentially revised to prevent further osteolysis.

TREATMENT OPTIONS AND CLINICAL OUTCOMES

It is important to remember that osteolysis is a biological phenomenon rather than a clinical condition. Osteolysis, in and of itself, is frequently an asymptomatic finding identified in routine postoperative imaging. For patients without clinical symptoms who present with imaging findings of mild osteolysis, nonoperative management with close follow-up is appropriate. Serial clinical and radiographic evaluations are recommended to identify the early development of symptoms and radiographic evidence of osteolysis progression or implant loosening.

Surgical management of osteolysis is reserved for patients who manifest clinical symptoms directly attributable to osteolysis and aseptic loosening, such as pain, dysfunction, or shoulder instability, in the absence of an active or indolent infection. A particular treatment strategy must consider (1) the size, location, and chronicity of osteolysis; (2) the suspected source of loosening (i.e., glenoid vs. humeral component, as well as component malpositioning); (3) the patient's primary subjective complaint; and (4)

the patient's functional status. The task of identifying an appropriate treatment is made challenging by the paucity of high-level, direct comparative studies of available treatment options. Given that the existing surgical treatments vary in invasiveness and the anticipated duration of recovery and that revision shoulder arthroplasty outcomes are generally inferior to the outcomes of primary arthroplasty, a shared decision-making process is essential to ensure that the chosen intervention matches the patient's goals and expectations (Fig. 1).

Management of Osteolysis and Aseptic Loosening Following Anatomical TSA

For patients with symptomatic osteolysis and evidence of glenoid loosening following anatomical TSA or RSA, nonoperative treatment is generally reserved only for patients that are poor surgical candidates and medically unfit for surgery. This approach relies on secondary stabilizers to maintain the functional integrity of the shoulder. To solidify the surrounding soft tissue architecture, nonoperative treatment consists of a 4–6-week period of sling immobilization during which active and passive range of motion are deferred. Whereas all surgical treatment options to be discussed in this article carry a significant risk for complications, non-surgical management mitigates the risk of surgery-related complications. In a retrospective analysis of 79 patients diagnosed with aseptic glenoid loosening following RSA, Lädermann et al. [53] demonstrated that a sub-group of 29 shoulders treated nonoperatively had similar clinical improvements and fewer associated complications compared to a group of 27 shoulders that underwent revision. Furthermore, in similar cohorts of patients, nonoperative treatment resulted in better clinical outcome scores than revision to hemiarthroplasty.

Arthroscopic Glenoid Polyethylene Removal

In postoperative anatomical TSA patients with isolated aseptic glenoid loosening and suspected infection, arthroscopic removal of the polyethylene glenoid component offers an appealing surgical option [54,55]. Given the high suspicion for periprosthetic infection and concurrent difficulty in diagnosing indolent *Cutibacterium acnes* infection in this clinical scenario, an arthroscopic procedure enables the clinician to obtain intraoperative tissue samples to aid in diagnosis while performing a minimally-invasive glenoid resection that may provide significant symptomatic relief. Removal of the polyethylene component reduces debris created by contact between the glenoid component and the adjacent metal and bone [54]. To address cavitory bone defects caused by prior osteolysis, bone graft, in the form of corticocancellous bone chips, can be introduced arthroscopically through

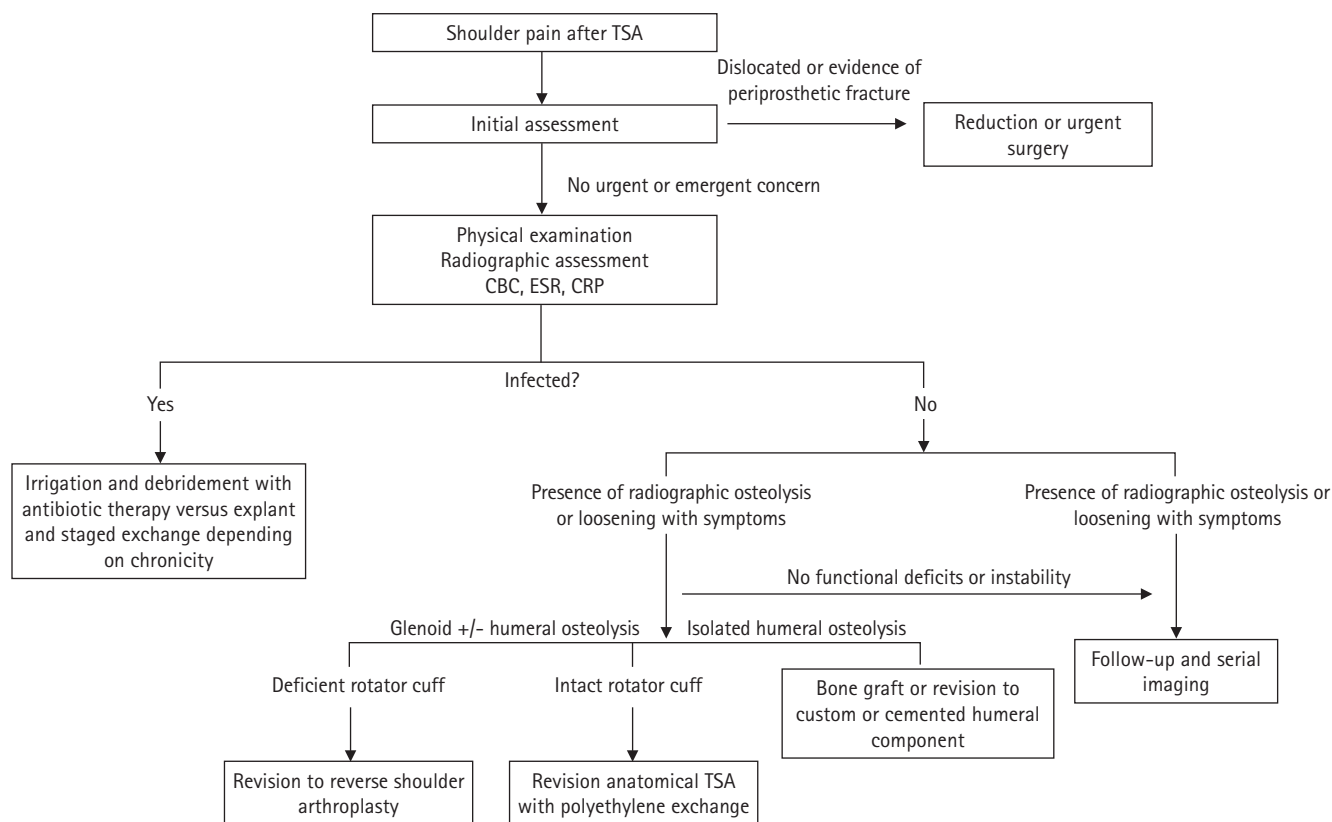


Fig. 1. Proposed treatment algorithm for the evaluation and management of patients with osteolysis after total shoulder arthroplasty (TSA). CBC: complete blood count, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein.

an enlarged anterosuperior portal and tamped into the glenoid cavity until the void is filled [56]. The use of a human dermal allograft patch has been described to help contain the bone graft within the defect [56]. Clinical outcome data regarding dermal allograft procedures have yet to be published. However, the available literature supports the use of isolated arthroscopic glenoid resection. Indeed, a cohort of 15 patients who underwent glenoid component resection with or without bone grafting had comparable pain relief and satisfaction at 2 years postoperatively in comparison to patients that underwent glenoid reimplantation [57]. Given that the authors noted a selection bias in that lower-demand patients were more likely to undergo an isolated glenoid component resection, further evidence is needed to delineate the optimal patient characteristics for this intervention. Nonetheless, in patients whose clinical presentation remains concerning but non-diagnostic for infection, an arthroscopic glenoid component resection with tissue culture procurement is a reasonable temporizing option.

Revision TSA with Polyethylene Glenoid Reimplantation

Another commonly employed surgical treatment option for aseptic glenoid loosening following anatomical TSA is revision

anatomical TSA with reimplantation of another polyethylene glenoid [58]. The greater potential shoulder range of motion conferred by an anatomical TSA, in comparison to that of an RSA, has made this an enticing revision option, particularly in younger patients [59,60]. In an early report of outcomes from this intervention, Cheung et al. [61] compared 33 shoulders with glenoid reimplantation to 35 shoulders with glenoid implant removal and bone grafting. Five-year postoperative outcome data demonstrated a 91% reoperation-free survival and higher satisfaction in patients that underwent reimplantation compared to those that underwent implant removal and bone grafting. However, in subsequent work, the authors conceded that these findings might have been confounded by the inclusion of infected arthroplasty cases in their analysis [62]. Subsequent studies have demonstrated that revision anatomical TSA indicated for glenoid loosening has been fraught with complications. In one analysis of 42 patients with symptomatic glenoid loosening following a primary anatomical TSA who underwent an isolated glenoid exchange, 67% of patients had recurrence of glenoid loosening, and 17% required reoperation at approximately year 6 of follow-up [63]. Sheth et al. [64] corroborated the disappointing results of revision anatomical TSA in a cohort of 20 patients, reporting that

35% required reoperation within 3 years of revision surgery. The poor clinical outcomes and increased complications associated with revision anatomical TSA and isolated glenoid component exchange make its contemporary use in the current treatment of glenoid component loosening relatively minimal.

Conversion to RSA

In the setting of a failed anatomical TSA due to osteolysis or glenoid component loosening, conversion to RSA affords several advantages over revision anatomical TSA (Fig. 2). Whereas anatomical TSA requires an intact and functioning rotator cuff for optimal outcomes, RSA outcomes can be satisfactory even with rotator cuff deficiency, which is often present in patients undergoing revision shoulder arthroplasty [65]. Second, on the glenoid side, RSA allows for both stronger fixation with screws and posts, as well as bony ingrowth for greater potential implant longevity [65]. Third, RSA allows the surgeon to not only address the aforementioned bone loss with the increasing popularity of augmented baseplates [66]. The available clinical evidence bores out these advantages. A multicenter study of 37 anatomical TSAs revised to RSA for aseptic glenoid loosening demonstrated an 86% patient satisfaction rate at approximately year 4 of follow-up [67]. The authors reported a 21% reoperation rate and, therefore, cautioned that, despite a high satisfaction rate, patients must be counseled on the elevated risks of reoperation compared with an index operation. Currently, RSA affords the most predictable surgical solution for symptomatic aseptic loosening and osteolysis following shoulder arthroplasty. Further elucidation of optimal patient candidates and long-term clinical outcomes of RSA used in this setting are needed.

Osteolysis Involving the Humeral Component

Humeral component loosening secondary to osteolysis surrounding the humeral implant is exceedingly rare. In a radiographic study of 395 shoulders that previously underwent either hemiarthroplasty or total arthroplasty, 43% of shoulders demonstrated evidence of osteolysis at either the greater tuberosity or calcar [48]. Despite this, humeral component loosening was not observed in any of the uncemented stems, and only one cemented stem was deemed to be at risk for humeral loosening based on the morphology of radiolucent lines surrounding the implant. In the single published case series on the management of humeral component aseptic loosening, Cil et al. [68] reported on 38 cases over a nearly 30-year period. The authors used cancellous bone grafting to treat contained proximal humerus osteolysis in approximately one-third of cases. Due to more extensive bone loss, custom humeral stem implants were employed in two cases. At revision, cement humeral fixation was utilized in approximately 75% of cases. Some authors postulate that the expanded use of stemless humeral implants in shoulder arthroplasty will further minimize the risk of proximal humerus osteolysis; however, further studies are needed to evaluate the impact of stemless humeral designs [69].

Management of Osteolysis and Aseptic Loosening Following RSA

There are limited data available to guide clinicians in the management of aseptic glenoid loosening following RSA. As mentioned, nonoperative treatment should be pursued as a first-line treatment option in minimally symptomatic patients. For patients unable to tolerate nonoperative management, glenoid loos-

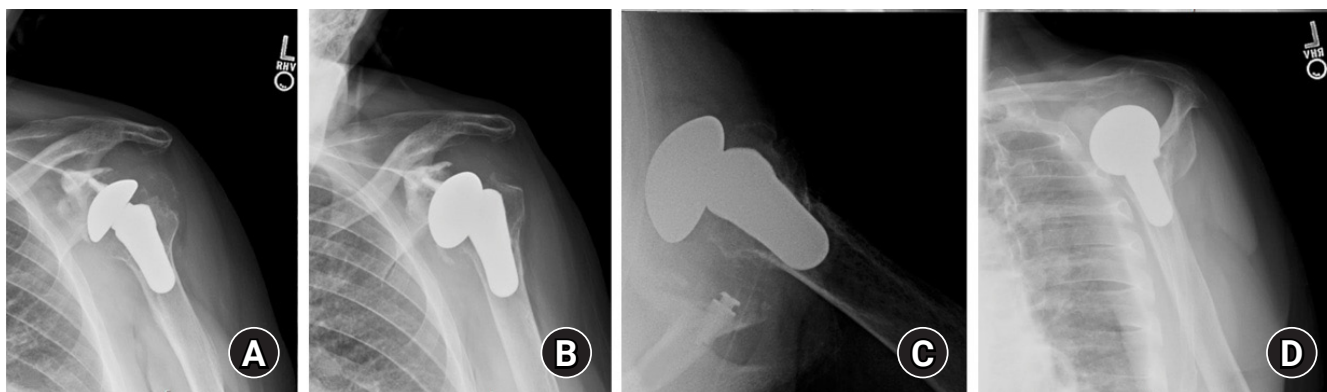


Fig. 2. Eighty-year-old male with a prior surgical history of left anatomical total shoulder arthroplasty (TSA) at an outside hospital in 2018 who presented with 3 years of increasing left shoulder pain and discomfort, especially with physical activity. Physical examination demonstrated the skin over the left shoulder to be intact, and a well-healed surgical incision was observed. The range of motion was 80° of forward flexion, 45° external rotation, and internal rotation to the L4 vertebrae. (A) Internal rotation, (B) external rotation, and (C) axillary, and (D) outlet radiographs at this time demonstrated a previous anatomical TSA with chronic bony remodeling of the glenoid and anterior dislocation of the humeral component with associated proximal humeral osteolysis. The patient was indicated to undergo conversion to an reverse shoulder arthroplasty.

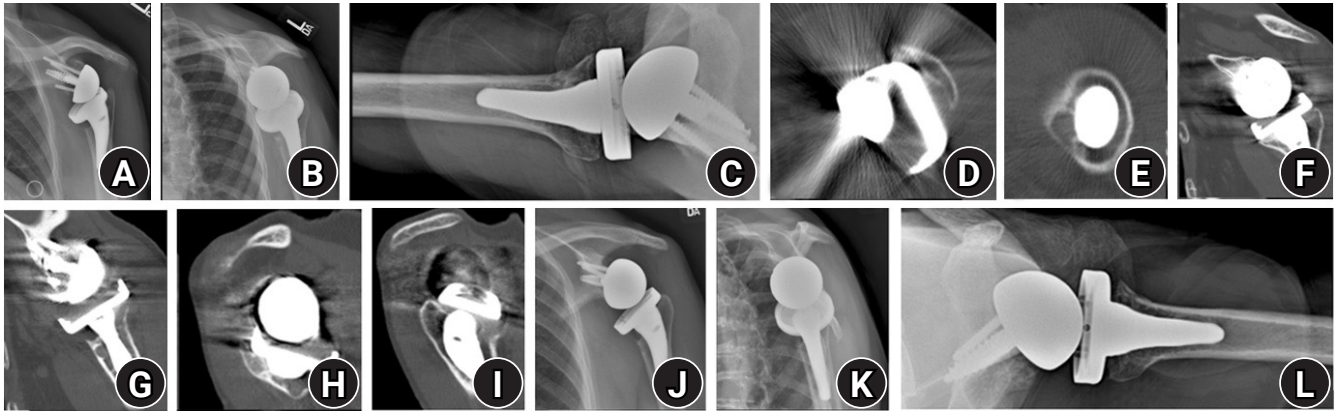


Fig. 3. Eighty-two-year-old healthy female with prior surgical history of a left reverse shoulder arthroplasty (RSA) at an outside hospital on September 24, 2017, and subsequent right RSA at an outside hospital on May 30, 2018, who presented with a chief complaint of left shoulder pain. She stated that the pain began 2 weeks prior to evaluation after being pulled by her dog while holding its leash. She localized the pain to the anterior aspect of the shoulder without radiation. Upon physical exam, the skin over the left shoulder was intact, and a well-healed surgical incision was noted. The range of motion was 140° of forward flexion, 45° of external rotation, and internal rotation to the L1 vertebrae. (A-C) Anteroposterior (A), internal rotation (B), and axillary (C) radiographs at that time demonstrated radiolucencies around the humeral stem and the glenoid baseplate. Though osteolysis was suspected, the decision was made to first rule out low-grade infection and further evaluate the shoulder with a computed tomography (CT) scan. Her erythrocyte sedimentation rate was 6 mm/hr, C-reactive protein level was 0.6 mg/L, and her white blood cell count was 6.8/nL which were not concerning for infection. (D-I) Evaluation of this CT scan on axial (D, E), coronal (F, G), and sagittal (H, I) views demonstrated two separate radiolucencies around the medial aspect of the proximal humeral component, which were concerning for osteolysis with aseptic loosening. On March 9, 2021, the patient underwent revision RSA with a Tornier Ascend Flex lateralized 36 glenosphere and +6 poly with centered 0 tray. (J-L) At 8-week postoperation, she was noted to be recovering well with forward flexion to 130°, external rotation to 30°, and acceptable component positioning on anteroposterior (J), internal rotation (K), and axillary (L) views.

ening should be treated with revision of the glenosphere. Lädermann et al. [53] reviewed 79 patients treated for aseptic glenoid loosening. Among this cohort, patients treated nonoperatively, and those treated with glenoid revision experienced similar improvements in pain, range of motion, and clinical outcomes scores at a minimum 2-year follow-up. As the number of RSA procedures continues to grow, so too will our collective experience with managing its associated complications, including osteolysis and aseptic loosening. A select example demonstrating our institutional experience with the management of osteolysis after RSA is described in Fig. 3.

CONCLUSION

Osteolysis following primary TSA is a challenging clinical entity that causes up to 80% of complications. The pathogenesis of osteolysis is a macrophage-mediated response to debris from the TSA construct that is further facilitated by micromotion. A thorough history and physical examination are essential to rule out other causes of symptomatic TSA—namely, periprosthetic joint infection. Though radiographs remain the gold standard imaging modality in this setting, they remain insensitive for detecting radiolucent lines and early osteolysis, with limited evidence suggesting that CT may be a more efficacious modality for diagnosis.

Once confirmed, nonoperative treatment of osteolysis should first be pursued given the potential to avoid surgery-associated risks, and limited data suggesting outcomes may be similar to that of reoperations. Current options for reoperations include glenoid polyethylene revision and conversion to RSA. Future studies are warranted to better define the indications and long-term outcomes of these procedures, though RSA currently appears to be the most reliable option given the evidence available.

ORCID

Kyle N. Kunze

<https://orcid.org/0000-0002-0363-3482>

REFERENCES

1. Wagner ER, Farley KX, Higgins I, Wilson JM, Daly CA, Gottschalk MB. The incidence of shoulder arthroplasty: rise and future projections compared with hip and knee arthroplasty. *J Shoulder Elbow Surg* 2020;29:2601-9.
2. van de Sande MA, Brand R, Rozing PM. Indications, complications, and results of shoulder arthroplasty. *Scand J Rheumatol* 2006;35:426-34.
3. Torchia ME, Cofield RH, Settergren CR. Total shoulder arthroplasty with the Neer prosthesis: long-term results. *J Shoulder*

- Elbow Surg 1997;6:495-505.
4. Sneppen O, Fruensgaard S, Johannsen HV, Olsen BS, Sojbjerg JO, Andersen NH. Total shoulder replacement in rheumatoid arthritis: proximal migration and loosening. *J Shoulder Elbow Surg* 1996;5:47-52.
 5. Bohsali KI, Wirth MA, Rockwood CA Jr. Complications of total shoulder arthroplasty. *J Bone Joint Surg Am* 2006;88:2279-92.
 6. Gregory TM, Boukebous B, Gregory J, Pierrart J, Masemjean E. Short, medium and long term complications after total anatomical shoulder arthroplasty. *Open Orthop J* 2017;11:1133-41.
 7. Zilber S, Radier C, Postel JM, Van Driessche S, Allain J, Goutalier D. Total shoulder arthroplasty using the superior approach: influence on glenoid loosening and superior migration in the long-term follow-up after Neer II prosthesis installation. *J Shoulder Elbow Surg* 2008;17:554-63.
 8. Bauer TW, Schils J. The pathology of total joint arthroplasty. II. Mechanisms of implant failure. *Skeletal Radiol* 1999;28:483-97.
 9. Kepler CK, Nho SJ, Bansal M, et al. Radiographic and histopathologic analysis of osteolysis after total shoulder arthroplasty. *J Shoulder Elbow Surg* 2010;19:588-95.
 10. González O, Smith RL, Goodman SB. Effect of size, concentration, surface area, and volume of polymethylmethacrylate particles on human macrophages in vitro. *J Biomed Mater Res* 1996;30:463-73.
 11. Horowitz SM, Doty SB, Lane JM, Burstein AH. Studies of the mechanism by which the mechanical failure of polymethylmethacrylate leads to bone resorption. *J Bone Joint Surg Am* 1993;75:802-13.
 12. Gelb H, Schumacher HR, Cuckler J, Ducheyne P, Baker DG. In vivo inflammatory response to polymethylmethacrylate particulate debris: effect of size, morphology, and surface area. *J Orthop Res* 1994;12:83-92.
 13. DeHeer DH, Engels JA, DeVries AS, Knapp RH, Beebe JD. In situ complement activation by polyethylene wear debris. *J Biomed Mater Res* 2001;54:12-9.
 14. Pizzoferrato A, Stea S, Sudanese A, et al. Morphometric and microanalytical analyses of alumina wear particles in hip prostheses. *Biomaterials* 1993;14:583-7.
 15. Boyle WJ, Simonet WS, Lacey DL. Osteoclast differentiation and activation. *Nature* 2003;423:337-42.
 16. Abu-Amer Y. NF- κ B signaling and bone resorption. *Osteoporos Int* 2013;24:2377-86.
 17. Resnick D, Weisman M, Goergen TG, Feldman PS. Osteolysis with detritic synovitis: a new syndrome. *Arch Intern Med* 1978;138:1003-5.
 18. Masuda T, Takahashi A. Orthopedic and histopathological study on "detritic synovitis" in cases of primary and revision to-tal hip arthroplasty. *Pathol Int* 2017;67:116-7.
 19. Perlman MD, Schor AD, Gold ML. Implant failure with particulate silicone synovitis (detritic synovitis). *J Foot Surg* 1990;29:584-8.
 20. Guild T, Onsen LT, Rivers M, Cheski R, Bear B, Izquierdo R. Detritic synovitis with osteolysis leading to pathologic fracture and deltoid avulsion following total shoulder arthroplasty. *J Shoulder Elb Arthroplast* 2018;2:1-5.
 21. Pilliar RM, Lee JM, Maniopoulos C. Observations on the effect of movement on bone ingrowth into porous-surfaced implants. *Clin Orthop Relat Res* 1986;(208):108-13.
 22. Jasty M, Bragdon C, Burke D, O'Connor D, Lowenstein J, Harris WH. In vivo skeletal responses to porous-surfaced implants subjected to small induced motions. *J Bone Joint Surg Am* 1997;79:707-14.
 23. Hopkins AR, Hansen UN, Bull AM, Emery R, Amis AA. Fixation of the reversed shoulder prosthesis. *J Shoulder Elbow Surg* 2008;17:974-80.
 24. Goodman SB. The effects of micromotion and particulate materials on tissue differentiation: bone chamber studies in rabbits. *Acta Orthop Scand Suppl* 1994;258:1-43.
 25. Sabesan VJ, Ackerman J, Sharma V, Baker KC, Kurdziel MD, Wiater JM. Glenohumeral mismatch affects micromotion of cemented glenoid components in total shoulder arthroplasty. *J Shoulder Elbow Surg* 2015;24:814-22.
 26. Bonnevalle N, Geais L, Müller JH; Shoulder Friends Institute, Berhouet J. Effect of RSA glenoid baseplate central fixation on micromotion and bone stress. *JSES Int* 2020;4:979-86.
 27. Lung TS, Cruickshank D, Grant HJ, Rainbow MJ, Bryant TJ, Bicknell RT. Factors contributing to glenoid baseplate micromotion in reverse shoulder arthroplasty: a biomechanical study. *J Shoulder Elbow Surg* 2019;28:648-53.
 28. Chebli C, Huber P, Watling J, Bertelsen A, Bicknell RT, Matsen F 3rd. Factors affecting fixation of the glenoid component of a reverse total shoulder prosthesis. *J Shoulder Elbow Surg* 2008;17:323-7.
 29. Hoenig MP, Loeffler B, Brown S, et al. Reverse glenoid component fixation: is a posterior screw necessary. *J Shoulder Elbow Surg* 2010;19:544-9.
 30. Chou J, Malak SF, Anderson IA, Astley T, Poon PC. Biomechanical evaluation of different designs of glenospheres in the SMR reverse total shoulder prosthesis: range of motion and risk of scapular notching. *J Shoulder Elbow Surg* 2009;18:354-9.
 31. Lewicki KA, Bell JE, Van Citters DW. Analysis of polyethylene wear of reverse shoulder components: a validated technique and initial clinical results. *J Orthop Res* 2017;35:980-7.
 32. Kohut G, Dallmann F, Irlenbusch U. Wear-induced loss of mass

- in reversed total shoulder arthroplasty with conventional and inverted bearing materials. *J Biomech* 2012;45:469-73.
33. Vaupel ZM, Baker KC, Kurdziel MD, Wiater JM. Wear simulation of reverse total shoulder arthroplasty systems: effect of glenosphere design. *J Shoulder Elbow Surg* 2012;21:1422-9.
 34. McLendon PB, Schoch BS, Sperling JW, Sánchez-Sotelo J, Schleck CD, Cofield RH. Survival of the pegged glenoid component in shoulder arthroplasty: part II. *J Shoulder Elbow Surg* 2017;26:1469-76.
 35. Fox TJ, Cil A, Sperling JW, Sanchez-Sotelo J, Schleck CD, Cofield RH. Survival of the glenoid component in shoulder arthroplasty. *J Shoulder Elbow Surg* 2009;18:859-63.
 36. Wirth MA, Klotz C, Deffenbaugh DL, McNulty D, Richards L, Tipper JL. Cross-linked glenoid prosthesis: a wear comparison to conventional glenoid prosthesis with wear particulate analysis. *J Shoulder Elbow Surg* 2009;18:130-7.
 37. Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR). Hip, knee and shoulder arthroplasty: annual report 2018. Adelaide, SA: AOANJRR; 2018.
 38. Gauci MO, Bonneville N, Moineau G, Baba M, Walch G, Boileau P. Anatomical total shoulder arthroplasty in young patients with osteoarthritis: all-polyethylene versus metal-backed glenoid. *Bone Joint J* 2018;100:485-92.
 39. Gulotta LV, Chambers KL, Warren RF, Dines DM, Craig EV. No differences in early results of a hybrid glenoid compared with a pegged implant. *Clin Orthop Relat Res* 2015;473:3918-24.
 40. Friedman RJ, Cheung E, Grey SG, et al. Clinical and radiographic comparison of a hybrid cage glenoid to a cemented polyethylene glenoid in anatomic total shoulder arthroplasty. *J Shoulder Elbow Surg* 2019;28:2308-16.
 41. Bell SN, Christmas MU, Coghlan JA. Proximal humeral osteolysis and glenoid radiolucent lines in an anatomic shoulder arthroplasty: a comparison of a ceramic and a metal humeral head component. *J Shoulder Elbow Surg* 2020;29:913-23.
 42. Barth J, Garret J, Geais L, et al. Influence of uncemented humeral stem proximal geometry on stress distributions and torsional stability following total shoulder arthroplasty. *J Exp Orthop* 2019;6:8.
 43. Razfar N, Reeves JM, Langohr DG, Willing R, Athwal GS, Johnson JA. Comparison of proximal humeral bone stresses between stemless, short stem, and standard stem length: a finite element analysis. *J Shoulder Elbow Surg* 2016;25:1076-83.
 44. Mueller U, Braun S, Schroeder S, et al. Influence of humeral head material on wear performance in anatomic shoulder joint arthroplasty. *J Shoulder Elbow Surg* 2017;26:1756-64.
 45. Moroder P, Gerhardt C, Renz N, Trampuz A, Scheibel M. Diagnostik und management des endoprotheseninfekts am schultergelenk. *Obere Extrem* 2016;11:78-87.
 46. Zmistowski B, Carpenter DP, Chalmers PN, Smith MJ, Keener JD. Symptomatic aseptic loosening of a short humeral stem following anatomic total shoulder arthroplasty. *J Shoulder Elbow Surg* 2021;30:2738-44.
 47. Khan A, Bunker TD, Kitson JB. Clinical and radiological follow-up of the Aequalis third-generation cemented total shoulder replacement: a minimum ten-year study. *J Bone Joint Surg Br* 2009;91:1594-600.
 48. Raiss P, Edwards TB, Deutsch A, et al. Radiographic changes around humeral components in shoulder arthroplasty. *J Bone Joint Surg Am* 2014;96:e54.
 49. Litchfield RB, McKee MD, Balyk R, et al. Cemented versus uncemented fixation of humeral components in total shoulder arthroplasty for osteoarthritis of the shoulder: a prospective, randomized, double-blind clinical trial: a JOINTs Canada Project. *J Shoulder Elbow Surg* 2011;20:529-36.
 50. Bacle G, Nové-Josserand L, Garaud P, Walch G. Long-term outcomes of reverse total shoulder arthroplasty: a follow-up of a previous study. *J Bone Joint Surg Am* 2017;99:454-61.
 51. Gregory T, Hansen U, Khanna M, et al. A CT scan protocol for the detection of radiographic loosening of the glenoid component after total shoulder arthroplasty. *Acta Orthop* 2014;85:91-6.
 52. Yian EH, Werner CM, Nyffeler RW, et al. Radiographic and computed tomography analysis of cemented pegged polyethylene glenoid components in total shoulder replacement. *J Bone Joint Surg Am* 2005;87:1928-36.
 53. Läderrmann A, Schwitzguebel AJ, Edwards TB, et al. Glenoid loosening and migration in reverse shoulder arthroplasty. *Bone Joint J* 2019;101:461-9.
 54. Venjakob AJ, Reichwein F, Nebelung W. Arthroscopic removal of a polyethylene glenoid component in total shoulder arthroplasty. *Arthrosc Tech* 2015;4:e149-52.
 55. O'Driscoll SW, Petrie RS, Torchia ME. Arthroscopic removal of the glenoid component for failed total shoulder arthroplasty: a report of five cases. *J Bone Joint Surg Am* 2005;87:858-63.
 56. Abildgaard JT, Bentley JC, Hawkins RJ, Tokish JM. Arthroscopic removal of a loose polyethylene glenoid component with bone grafting and patch augmentation for glenoid osseous defect. *Arthrosc Tech* 2017;6:e529-35.
 57. Raphael BS, Dines JS, Warren RF, et al. Symptomatic glenoid loosening complicating total shoulder arthroplasty. *HSS J* 2010;6:52-6.
 58. Deutsch A, Abboud JA, Kelly J, et al. Clinical results of revision shoulder arthroplasty for glenoid component loosening. *J Shoulder Elbow Surg* 2007;16:706-16.

59. Kiet TK, Feeley BT, Naimark M, et al. Outcomes after shoulder replacement: comparison between reverse and anatomic total shoulder arthroplasty. *J Shoulder Elbow Surg* 2015;24:179-85.
60. Muh SJ, Streit JJ, Wanner JP, et al. Early follow-up of reverse total shoulder arthroplasty in patients sixty years of age or younger. *J Bone Joint Surg Am* 2013;95:1877-83.
61. Cheung EV, Sperling JW, Cofield RH. Revision shoulder arthroplasty for glenoid component loosening. *J Shoulder Elbow Surg* 2008;17:371-5.
62. Aibinder WR, Schoch B, Schleck C, Sperling JW, Cofield RH. Revisions for aseptic glenoid component loosening after anatomic shoulder arthroplasty. *J Shoulder Elbow Surg* 2017;26:443-9.
63. Bonnevalle N, Melis B, Neyton L, et al. Aseptic glenoid loosening or failure in total shoulder arthroplasty: revision with glenoid reimplantation. *J Shoulder Elbow Surg* 2013;22:745-51.
64. Sheth M, Sholder D, Padegimas EM, et al. Failure of anatomic total shoulder arthroplasty with revision to another anatomic total shoulder arthroplasty. *Arch Bone Jt Surg* 2019;7:19-23.
65. Goetti P, Denard PJ, Collin P, Ibrahim M, Mazzolari A, Lädermann A. Biomechanics of anatomic and reverse shoulder arthroplasty. *EFORT Open Rev* 2021;6:918-31.
66. Hernandez NM, Chalmers BP, Wagner ER, Sperling JW, Cofield RH, Sanchez-Sotelo J. Revision to reverse total shoulder arthroplasty restores stability for patients with unstable shoulder prostheses. *Clin Orthop Relat Res* 2017;475:2716-22.
67. Melis B, Bonnevalle N, Neyton L, et al. Glenoid loosening and failure in anatomical total shoulder arthroplasty: is revision with a reverse shoulder arthroplasty a reliable option. *J Shoulder Elbow Surg* 2012;21:342-9.
68. Cil A, Veillette CJ, Sanchez-Sotelo J, Sperling JW, Schleck C, Cofield RH. Revision of the humeral component for aseptic loosening in arthroplasty of the shoulder. *J Bone Joint Surg Br* 2009;91:75-81.
69. Churchill RS, Athwal GS. Stemless shoulder arthroplasty-current results and designs. *Curr Rev Musculoskelet Med* 2016;9:10-6.